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Survey On Prevalence And Pharmacological Approaches In Non-Alcoholic Fatty Liver Disease And Steatohepatitis

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ABSTRACT

Introduction: Non-Alcoholic Fatty Liver Disease and Non-Alcoholic Steatohepatitis have emerged as significant public health concerns, closely linked to metabolic syndrome. This study aimed to assess the prevalence, associated risk factors, and pharmacological approaches for managing NAFLD/NASH.

Material And Methods: A cross-sectional study was conducted on 191 adult patients diagnosed with NAFLD or NASH based on clinical assessments, laboratory parameters, and imaging findings. Data on demographics, comorbidities, pharmacological treatments, and biochemical markers were analyzed to evaluate disease severity and treatment patterns.

Results: NAFLD was most prevalent among middle-aged adults (40–50 years), with a male predominance. Obesity (46.07%) and overweight status (30.36%) were the most common risk factors. Fibroscan findings indicated that 49.73% of patients had moderate fibrosis, while 17.80% had severe fibrosis. Elevated aspartate aminotransferase(AST),alanine aminotransferase(ALT), and ferritin levels were significantly associated with fibrosis severity. Pharmacological management predominantly involved vitamin E (46.07%), atorvastatin (43.97%), metformin (25.65%), and GLP-1 receptor agonists (29.84%), reflecting a growing focus on metabolic modulation in NAFLD treatment.

Conclusion: The study reinforces the strong association between NAFLD and metabolic dysfunction. While no FDA-approved treatment exists, the current therapeutic landscape relies on insulin sensitizers, lipid-lowering agents, and antioxidants. Early diagnosis and intervention through metabolic control remain crucial in mitigating disease progression. Further research is warranted to establish standardized treatment guidelines and assess long-term outcomes of pharmacological interventions.

Keywords: *Insulin Resistance, Non-Alcoholic Fatty Liver Disease, Non-Alcoholic Steatohepatitis, NAFLD, Metabolic Syndrome, Pharmacological Management.*

1. INTRODUCTION

Hepatic steatosis is a key feature of NAFLD, excluding cases caused by alcohol or other hepatotoxic substances. NAFLD, now the leading cause of chronic liver disease worldwide, progresses due to lipotoxicity, oxidative stress, and lipid accumulation[1]. It encompasses a spectrum of conditions, including NAFL and NASH, differentiated by histological findings. Defined by steatosis in over 5% of hepatocytes, NAFLD is closely linked to metabolic disorders like obesity and type 2 diabetes[2]. First termed by Schaffner in 1986, the disease contributes to insulin resistance, with a notably higher prevalence among individuals with T2DM[3,4].

NAFLD encompasses various pathological conditions, necessitating tailored treatment strategies. Its progression includes simple fatty liver, steatohepatitis, fibrosis, cirrhosis, and potential hepatocellular carcinoma[5]. Despite its complexity, NAFLD is preventable by addressing key risk factors[6].In Europe, NAFLD prevalence ranges from 2% to 44%, even among obese children, with type 2 diabetes affecting 42.6% to 69.5%. Compared to other ethnic groups, Indians show higher insulin

resistance and hepatic lipid content. As a metabolic syndrome manifestation, NAFLD awareness is rising, though standardized diagnostic criteria remain lacking[5].

NAFLD prevalence remains uncertain in India, though obesity is strongly linked to fatty liver, with 91% of obese individuals showing signs on ultrasonography[7-9]. The AST-ALT ratio helps differentiate NAFLD from alcoholic liver disease. Rising obesity, diabetes, and insulin resistance may contribute to increasing NAFLD cases. Key risk factors include obesity, type 2 diabetes, dyslipidemia, hypertension, and cyclic weight loss, which also elevate cardiovascular disease risk. Managing NAFLD requires addressing underlying metabolic conditions[10]. While excess triglyceride accumulation leads to hepatocyte enlargement and inflammation, the disease progression differs between NAFLD and alcoholic liver disease[11].

The PNPLA3 GG variant in NASH patients is linked to higher AST levels and advanced fibrosis compared to the CC variant[12]. Insulin resistance plays a key role in NAFLD/NASH development, but insulin sensitizers can enhance hepatic insulin sensitivity and liver function. Pioglitazone, a type 2 diabetes drug, improves insulin signaling, enhances fat and glucose metabolism, and lowers hepatic gluconeogenesis. It also mitigates hepatic steatosis and inflammation by modulating PPARγ signaling and mitochondrial gene expression[13-15].

Additionally, NASH progression and fibrosis involve both canonical and non-canonical Wnt signaling pathways[16].The tumour suppressor gene p53 plays a key role in NAFLD and NASH progression. Studies indicate that GLP-1 agonists do not lower NAFLD risk compared to insulin. Various miRNAs influence NAFLD/NASH by modulating signaling pathways[17]. Among treatments, vitamin E and pioglitazone have shown the most effectiveness[18].No medication is specifically approved for NAFLD treatment. However, drugs for metabolic syndrome conditions like diabetes and dyslipidemia are often used[19]. Since neither the USFDA nor EMA has authorized a specific NAFLD drug, its treatment relies on off-label use of existing medications[20].Clinical studies for NAFLD have involved treatments with pioglitazone for 6–36 months and vitamin E for 6–24 months[21-22].

Many NAFLD patients also experience hypertension and are often overweight[24-25]. Physical exams frequently reveal hepatomegaly[26]. Biochemically, these patients may show impaired insulin sensitivity, hyperglycemia, hyperinsulinemia, and hyperlipidemia. Aminotransferases are typically mildly elevated, with an AST/ALT ratio of less than 1, unless cirrhosis is present. Serum aminotransferase levels vary with disease progression[23,27-29]. Histologically, NAFLD with normal aminotransferases may show benign steatosis or cirrhosis[30].Gamma-glutamyl transpeptidase (GGT) levels may be elevated in NAFLD patients but are not reliable for diagnosing NASH[31,32].

Ferritin levels are often increased and could indicate severe fibrosis, inflammation, or steatosis[33-34]. While imaging techniques like MRI, CT, and ultrasound are helpful for detecting NAFLD, they cannot distinguish between benign steatosis and NASH[35-36]. MRI can accurately measure liver triglyceride content but is costly. Various treatments for disease progression, including PUFA supplementation, vitamin E, thiazolidinediones, and statins, target the pathophysiological mechanisms, focusing on lipid peroxidation, diabetes, and dyslipidemia[37-38].

2. MATERIALS AND METHODS

Study Design and Setting

This was a multicenter, observational study conducted at two medical institutions:The study aimed to evaluate the prevalence of comorbidities and pharmacological treatment strategies in patients diagnosed with NAFLD and NASH. Data were collected retrospectively from patients' medical records over a six-month period.

Study Population

A total of 191 patients, both male and female, with confirmed diagnoses of NAFLD or NASH, were included in the study. Patients were selected based on the following criteria:

Inclusion Criteria

- Patients of all ages and both genders, with a confirmed diagnosis or suspected diagnosis of NAFLD or NASH, were eligible for inclusion in the study.
- Patients with any form of hepatic disease.

Exclusion Criteria

- Patients unwilling to participate or unable to provide informed consent.
- Pregnant women diagnosed with NAFLD or NASH.

Data Collection

Data were obtained using a structured patient data collection form, which included information on demographics (age, gender), BMI, medical history, comorbid conditions, laboratory investigations, and treatment details. Data were gathered from the patients' OPD records, hospital medical files, and laboratory reports.

Assessment of Comorbidities

Comorbid conditions such as hypertension, diabetes mellitus, hyperlipidemia, hypertriglyceridemia, hypothyroidism, and hyperthyroidism were documented. Additionally, the presence of diabetic dyslipidemia and other metabolic disorders was noted.

Liver Function and Fibrosis Assessment

Liver function was evaluated using laboratory markers, including AST and ALT levels. Fibrosis was assessed using non-invasive methods, primarily Fibroscan and ultrasound, to categorize patients into mild (F1), moderate (F2), and severe fibrosis (F3) groups. These scores were further corroborated by ultrasound findings indicating the severity of fatty infiltration in the liver.

Pharmacological Treatment

The study also evaluated the pharmacological treatment strategies employed in the management of NAFLD and NASH. The medications used were categorized as hypolipidemic agents, antioxidants, and antidiabetic medications.

Data Analysis

Data were entered into Microsoft Excel and analyzed using a combination of descriptive and inferential statistics. Descriptive statistics, including counts, percentages, and mean values, were utilized to provide an overarching summary of categorical and continuous variables across the study population.

Ethical Considerations

Ethical approval for the study was obtained from the Institutional Ethics Committee PUIECHR/PIMSR/00/081734/6501. The study was conducted following the ethical guidelines for biomedical research involving human subjects, and informed consent was obtained from all patients before data collection.

3. RESULTS

1. Age-wise distribution of patients:

The following table presents the distribution of NAFLD/NASH patients across different age groups, along with a breakdown by gender. The highest prevalence is observed in individuals aged 40–50 years, highlighting middle-aged adults as the most affected demographic. This finding aligns with existing literature indicating that metabolic dysfunction, which increases with age, contributes to the pathogenesis of NAFLD/NASH.

Table 1. Age-wise distribution of patients

Age Group (years)	Male	Female	Total Patients (n=191)	MEAN VALUE
<30	18(9.42%)	20(10.47%)	38	$\bar{X}$ =38.2
30-40	27(14.13%)	25(13.08%)	52	
40-50	36(18.84%)	28(14.65%)	64	
50-60	11(5.75%)	14(7.32%)	25	
> 60	8(4.18%)	4(2.09%)	12	

2. Comorbidities in patients diagnosed

The following table outlines the prevalence of common comorbidities associated with NAFLD/NASH, including diabetes mellitus (DM), hypertension (HTN), dyslipidemia, hypertriglyceridemia, obesity, and overweight status. Obesity (46.07%) and overweight status (30.36%) emerge as the most significant risk factors, reinforcing their role in hepatic lipid accumulation and disease progression. The high prevalence of metabolic disorders among these patients underscores the need for comprehensive metabolic control in NAFLD management.

Table 2. Comorbidities in patients diagnosed

Comorbidities	Male	Female	Total Patients (n=191)	MEAN VALUE
DM	34(17.80%)	25(13.08%)	59	$\bar{X}$ =31.83
HTN	31(16.23%)	22(11.51%)	53	
Dyslipidemia	45(23.56%)	33(17.27%)	78	
Hypertriglyceridemia	21(10.99%)	24(12.56%)	45	
Obese	46(24.08%)	42(21.98%)	88	
Over Weight	58(30.36%)	45(23.56%)	103	

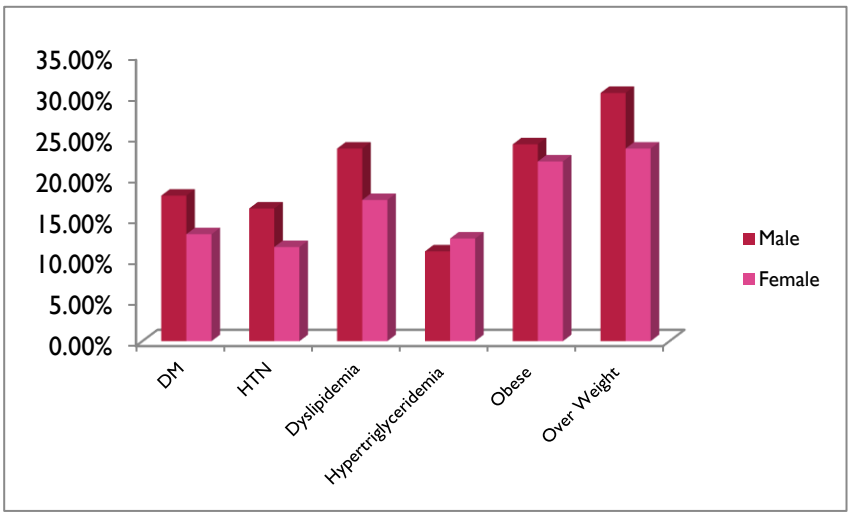

Figure 1. Comorbidities in patients diagnosed

3. Fibroscan results categorizing liver fibrosis severity

The following table categorizes patients based on Fibroscan findings into mild, moderate, and severe fibrosis stages. A considerable proportion of patients (49.73%) exhibit moderate fibrosis, while 17.80% present with severe fibrosis. These results highlight the progressive nature of NAFLD and the potential risk for cirrhosis, emphasizing the importance of early intervention to prevent advanced hepatic fibrosis.

Table 3. Fibroscan results categorizing liver fibrosis severity

Fibroscan	Percentage	Total Patients (n=191)	MEAN VALUE
Mild	32.46%	62	$\bar{X}$ =63.67
Moderate	49.73%	95	
Severe	17.80%	34	

4. Pharmacological treatments used

The following table summarizes the pharmacological agents prescribed for NAFLD/NASH management, including antioxidants, lipid-lowering agents, and insulin sensitizers. The most frequently prescribed medications are vitamin E (46.07%), atorvastatin (43.97%), metformin (25.65%), and GLP-1 receptor agonists such as liraglutide (29.84%) and semaglutide (23.56%). These findings reflect the evolving therapeutic landscape, where metabolic modulation remains a cornerstone in NAFLD treatment, despite the lack of FDA-approved pharmacological interventions.

Table 4. Pharmacological treatments used

Drugs	Percentage	No. of Patients
metformin	25.65%	49
Udi-hep	40.83%	78
Atorvastatin	43.97%	84
Liraglutide	29.84%	57
Vit-E	46.07%	88
Saroglitazar	19.89%	38
Pioglitazone	22.51%	43
Rosuvastatin	17.27%	33
semaglutide	23.56%	45

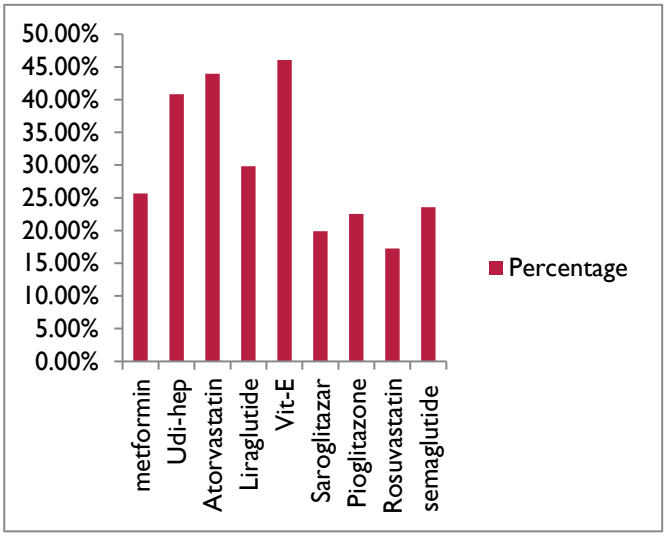

Figure 2. Pharmacological treatments used

5. Biochemical Parameters and Their Association with Fibrosis Severity

This table presents an overview of key biochemical markers, including triglycerides, ferritin, AST, ALT, and HbA1c levels, and their correlation with NAFLD severity. A significant proportion of patients exhibit elevated liver enzymes and dysregulated glucose metabolism, reinforcing their role in disease progression. Patients with severe fibrosis demonstrate markedly higher levels of these biomarkers, indicating that hepatic injury and metabolic disturbances exacerbate fibrosis. These findings highlight the necessity of biochemical monitoring for early diagnosis, risk stratification, and timely metabolic intervention to prevent disease progression.

Table 5. Biochemical parameters

Laboratory Reports			MEAN VALUE
Triglycerides			
100-200	15.70%	30	$\bar{X}$ =38.2
200-300	37.69%	72	
300-400	19.37%	37	

400-500	14.65%	28	
>500	12.56%	24	
Total	**100%**	**N=191**	
Ferritin			
100-200	27.22%	52	$\bar{X}$ =63.66
200-300	39.79%	76	
300-400	34.03%	65	
Total	**100%**	**N=191**	
AST			
<50	16.23%	31	$\bar{X}$ =47.75
50-60	36.12%	69	
60-70	32.46%	62	
>70	15.18%	29	
Total	**100%**	**N=191**	
ALT			
50-60	8.37%	16	$\bar{X}$ =38.2
60-70	24.08%	46	
70-80	30.36%	58	
80-90	24.08%	46	
>90	13.08%	25	
Total	**100%**	**N=191**	
HbA1c			
<6	28.79%	55	$\bar{X}$ =63.66
Between 6-7	49.21%	94	
>7	21.98%	42	
Total	**100%**	**N=191**	

Parameter	**Mild**	**Moderate**	**Severe**
AST	48(25.13%)	84(43.97%)	59(30.89%)
ALT	43(22.51%)	89(46.59%)	59(30.89%)
Triglycerides	60(31.41%)	78(40.83%)	53(27.74%)
Ferritin	52(27.22%)	76(39.79%)	65(34.03%)
HbA1c	55(28.79%)	94(49.21%)	42(21.98%)

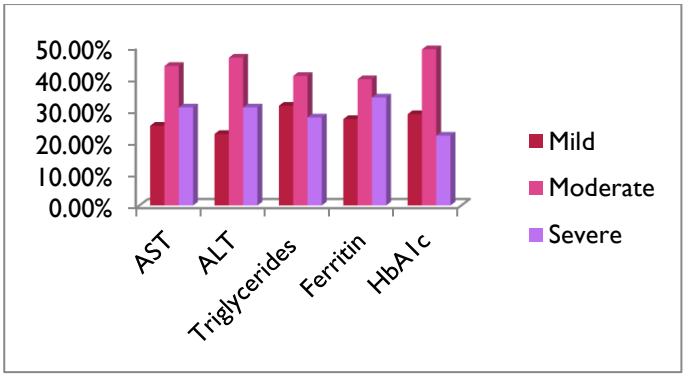

Figure 3. Biochemical parameters

4. DISCUSSION

The findings of this study underscore the significant burden of Non-Alcoholic Fatty Liver Disease (NAFLD) and Non-Alcoholic Steatohepatitis (NASH) within the study population, reflecting a growing global prevalence. This trend aligns with previous epidemiological studies indicating that NAFLD prevalence is closely associated with metabolic disorders such as obesity, type 2 diabetes mellitus (T2DM), dyslipidemia, and hypertension. The predominance of NAFLD in middle-aged adults, particularly those aged 40–50 years, reinforces the role of metabolic dysfunction in disease progression.

The higher prevalence among males compared to females could be attributed to differences in lifestyle, hormonal influences, and metabolic risk factors. The high incidence of obesity (46.07%) and overweight status (30.36%) among patients underscores the role of excess adiposity in hepatic steatosis. Obesity-related insulin resistance leads to hepatic lipid accumulation, oxidative stress, and inflammation, contributing to disease progression from simple steatosis to NASH.

The presence of metabolic comorbidities, including diabetes (30.89%) and hypertension (27.74%), further supports the association between metabolic syndrome and NAFLD. These findings are consistent with global studies emphasizing metabolic dysfunction as the primary driver of NAFLD development[39].

Fibroscan analysis revealed that nearly half of the patients (49.73%) had moderate fibrosis, while 17.80% exhibited severe fibrosis, suggesting a significant proportion of individuals at risk for cirrhosis and related complications. The correlation between fibrosis severity and biochemical markers, including elevated AST, ALT, and ferritin levels, indicates that hepatic injury and inflammation are integral to disease progression. The observed increase in HbA1c levels with advancing fibrosis severity suggests a strong link between glycemic control and NAFLD progression, reinforcing the need for comprehensive metabolic management in affected individuals. Pharmacological interventions were diverse, with vitamin E (46.07%) and atorvastatin (43.97%) being the most frequently prescribed agents. The use of vitamin E aligns with its known antioxidant properties, which help reduce hepatic inflammation and steatosis in NASH patients. This is supported by meta-analyses confirming the efficacy of vitamin E supplementation in improving liver function and histologic changes in patients with NAFLD and NASH[40]. Statins, widely used for dyslipidemia, may offer additional hepatoprotective benefits by modulating lipid metabolism and reducing cardiovascular risk. Studies have demonstrated that statin therapy can improve liver steatosis and reduce the expression of fibrotic genes in NAFLD patients[41]. The significant use of insulin sensitizers, including metformin (25.65%) and pioglitazone (22.51%), highlights the therapeutic focus on improving insulin sensitivity and reducing hepatic fat accumulation.

The inclusion of GLP-1 receptor agonists such as liraglutide (29.84%) and semaglutide (23.56%) suggests a growing interest in novel therapies targeting both metabolic and hepatic pathways in NAFLD.The study findings emphasize the need for early identification and targeted interventions for NAFLD patients, particularly those with metabolic comorbidities. The absence of an approved pharmacological treatment for NAFLD necessitates a multifaceted approach that includes lifestyle modifications alongside pharmacotherapy. Given the progressive nature of NAFLD, further longitudinal studies are required to assess the long-term impact of pharmacological treatments on disease progression and clinical outcomes[42].

5. CONCLUSION

The study highlights the increasing prevalence of NAFLD and NASH, with a significant correlation to metabolic disorders such as obesity, type 2 diabetes, and dyslipidemia. The findings confirm that middle-aged adults, particularly males, are at a higher risk, with nearly half of the study population exhibiting moderate fibrosis. The association between fibrosis severity and elevated biochemical markers, such as AST, ALT, and ferritin, underscores the need for early identification and risk stratification.

Pharmacological management primarily included vitamin E, atorvastatin, metformin, and GLP-1 receptor agonists, reflecting an evolving therapeutic approach targeting hepatic steatosis and metabolic dysfunction. The absence of an FDA-approved

treatment for NAFLD emphasizes the necessity for a multimodal strategy integrating pharmacological and lifestyle interventions. Given the progressive nature of NAFLD, further prospective studies are required to assess long-term treatment outcomes and the effectiveness of emerging therapies.

The findings underscore the urgent need for improved screening and early intervention strategies in high-risk individuals. Public health initiatives promoting metabolic health, lifestyle modifications, and targeted pharmacotherapy could mitigate the rising burden of NAFLD and its complications.

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